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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,432	WAUGH ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *5-9,13,14,18,22 and 28-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,10-12,15-17,19-21,23-27 and 39* is/are rejected.

7)☐ Claim(s) *2-4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 12/7/05.

Claims 1-39 are pending. In the response filed 8/8/05, Applicant elected group 1 and the species of a composition comprising a non-covalent association complex of a positively charged backbone polymer having positively charged branching groups of the formula $(gly)_p$-RGRDDRRQRRR-$(gly)_q$ (SEQ ID NO:19), a negatively charged backbone comprising a plurality of attached targeting moieties, and a negatively-charged backbone having a plurality of attached BOTOX molecules. Claims 1-4, 10, 11, 12, 15-17, and 39 read on this species, and the species was found to be free of the art

At page 11 of the response Applicant requested rejoinder of claims 2-4, 13, 14, and 18, arguing that these claims read on the originally elected species. This is persuasive with regard to claims 2-4 and these claims have been rejoined. It is not persuasive with regard to claim 13, 14, and 18. Claims 13 and 14 are drawn to species in which the positively charged branching groups are subspecies of non-elected species SEQ ID NO: 9, and claim 18 requires that the positively charged branching groups are either GGGRRRRRRR (SEQ ID NO:1) or HIV TAT. In contrast, the elected invention requires $(gly)_p$-RGRDDRRQRRR-$(gly)_q$ (SEQ ID NO:19) as a positively charged branching group. Note that the restriction requirement clearly indicated that non-identical positively charged fragments of TAT were considered to be patentably distinct species. See page 3, item '4' of the requirement mailed 5/19/04. So, the positively charged branching groups of claims 13, 14, and 18 are not considered to read on the elected species. For these reasons claims 13, 14, and 18 have not been rejoined.

After further search it has been determined that embodiments of the invention comprising a plurality of therapeutic or cosmeceutical agents listed in the specification, including BOTOX (botulinum toxin) molecules, attached to a negatively charged backbone and complexed with a positively charged backbone and a second negatively charged backbone (claims 2-4) are free of the art of record.

The Office has selected another species for consideration, i.e. a composition comprising a non-covalent association complex of a positively charged backbone that is a peptide comprising a positively charged branching group that is a fragment of HIV-TAT, at least one member selected from the group consisting of RNA, DNA, ribozymes, modified oligonucleotides and cDNA encoding a selected transgene, and DNA encoding at least one persistence factor, wherein the fragment of HIV-TAT is other than:

1. $G_{n1}R_{n2}$ with n1 = an integer from about 0 to about 20, and n2 = an odd integer from about 5-25,

2. G_p-RGRDDRRQRRR-G_q, (SEQ ID NO:19), and

3. G_p-YGRKKRRQRRR- G_q, (SEQ ID NO:20), as set forth in the restriction requirement of 5/19/04.

Claims 1, 10-12, 15-17, 19-21, 23-27, and 39 read on this species.

Claims 1, 2-4, 10-12, 15-17, 19-21, 23-27 and 39, are under consideration in this Office Action..

Rejections Withdrawn

The rejection of claims 1, 39, and dependents under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendment deleting "first", "second" and "third" from the claims.

The rejection of claims 15-17 under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendment.

The rejection of claims 19, 20, and 23-27 under 35 USC 112, second paragraph is withdrawn.

Claim Objections

Claim 12 is objected to because the phrase "groups comprises" lacks proper subject-verb agreement.

Claim 15 is objected to because the phrase "group are" lacks proper subject-verb agreement.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 19, 20, and 23-27 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because it is unclear what is intended by the term "length". The specification does not define this term and it is not clear what standard should be used to determine length. One standard that could be used is the length of the backbone in angstroms, another is the length of the backbone in terms of the number of monomers comprised, still another is the length of the backbone after it has folded as a result of interactions with the other members of the complex. It is also unclear if, in the situation where a complex comprises more than one of a given negatively charged backbone, all of the copies of that backbone should be used in the calculation. Because one of skill does not know which standard to apply, or what are the limits of how the length calculations can be performed, one cannot know the intended metes and bounds of the claims.

Response to Arguments

Applicant's arguments filed 12/7/05 have been fully considered but they are not persuasive.

With regard to claim 10, Applicant argues in the paragraph bridging pages 13 and 14 of the response that one would know that the term "length" refers to the number of repeating units in a chain, and not to its length in angstroms or any other measure. Applicant relies for support on the specification at page 7, lines 28-32 which reads:

> The sidechain moieties in this group of embodiments can be placed at spacings along the backbone that are consistent in separations or variable. Additionally, the length of the sidechains can be similar or dissimilar. For example, in one group of embodiments, the sidechains can be linear or branched hydrocarbon chains having from one to twenty carbon atoms and terminating at the distal end (away from the backbone) in one of the above-noted positively charged groups.

This provides support for measuring length in terms of the number of carbon atoms in a chain, however, it does not provide any limiting definition of the claim term "length". There is no reason, based on this passage, to limit the interpretation the term "length" to the definition supplied by Applicant in the response. As a result, Applicant's argument is unpersuasive and the rejection is maintained.

Applicant also argues that one of ordinary skill in the art would understand that only a single copy of a particular group (b) member should be used to calculate the length of the positively charged backbone required in claim 10, because one could not predict, prior to mixing the positively and negatively charged backbones together, the exact number of negatively charged group (b) members of a particular type that would associate with a given positively charged backbone. This argument is unpersuasive because it is only opinion and lacks any evidentiary support. Claim 10 is drawn to a noncovalent association complex of a positively charged backbone and at least two group (b) negatively charged backbones in which said positively charged backbone has a length of from about 1 to about 4 time the combined lengths of the negatively charged backbones. There is no basis in the claim for limiting the calculation by using only one member of each particular set of negatively charged backbones. On what basis can Applicant exclude the embodiment wherein the positively charged backbone is long enough and is present in sufficient molar excess, relative to the negative backbones, to bind all of the negative backbones in solution, including a plurality of each type, and still satisfy the length limitation?

New Matter

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 as originally filed contained the clause "group consisting of -$(gly)_n$-arg-arg-arg-arg-arg-arg-arg, HIV-TAT and fragments thereof,". In the response filed 12/7/05, a comma was inserted between "HIV-TAT" and "and fragments thereof". This has the effect of rendering the "and fragments thereof" limitation applicable to both $(gly)_n$-arg-arg-arg-arg-arg-arg-arg and HIV-TAT, whereas previously the claim did not embrace fragments of -$(gly)_n$-arg-arg-arg-arg-arg-arg-arg . The specification supports only fragments of -$(gly)_n$-arg-arg-arg-arg-arg-arg-arg that vary in the number of gly residues. The specification does not support fragments of -$(gly)_n$-arg-arg-arg-arg-arg-arg-arg with less than 7 arg residues. To the extent that the amended claim embraces fragments with less than 7 arg residues it contains new matter. Applicant is reminded that 37 CFR 1.121 sets for the proper manner of making amendments to the claims, and requires that the claims be marked up to show amendments. Insertion of the comma was not indicated by appropriate markings.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejection of claim 19-21 is applied to a generic form of the claims that is not limited to the species under consideration. This rejection demonstrates the unpatentability of the generic claims not limited to a species.

Claims 19-21 stand rejected under 35 U.S.C. 102(b) as being anticipated by Illum (US Patent 5,744,166).

Illum taught non-covalent complexes of polycations and nucleic acids. One exemplary polycation is polylysine modified with polyethylene glycol (PEG). See abstract; column 3, lines 16-19 and 57; and column 4, lines 4-7. PEG is considered to be an "efficiency group", as per claim 19.

Thus Illum anticipates the claims.

The following rejections address the species under consideration.

Claims 1, 11, 12, 19-21, 23, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al (J. Biol. Chem. 262(10): 4429-4432, 1987) as evidenced by GenBank Accession No. M77788 (2005).

Wu taught non-covalent complexes of plasmid pSV2 CAT and polylysine, wherein the polylysine comprised an attached asialoorosomucoid targeting ligand. See abstract. The targeting ligand is considered to be an "efficiency group", as per claim 19. Plasmid pSV2 CAT comprises a selectable marker (beta lactamase, i.e. ampicillin resistance) as evidenced by GenBank Accession No. M77788. The selectable marker is considered to be a persistence factor as required by claim 1. Regarding claims 11, 12 and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e. domains, which are also present in HIV-TAT because lysine is present in HIV TAT.

Thus Wu anticipates the claims.

Claims 1, 11, 12, 19-21, 23, 24, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Cristiano et al (Proc. Nat. Acad. Sci. USA 90: 11548-11552).

Cristiano taught non-covalent complexes of polylysine and plasmid pCMV betaGal. The polylysine comprised attached targeting ligands, e.g. adenovirus and asialoorosomucoid. See abstract. The plasmid comprised a beta galactosidase reporter gene under control of a CMV promoter. See page 11548, column 2, second full paragraph. Plasmid pCMV beta gal comprises a selectable marker considered to be a persistence factor as required by claim 1. Regarding claims 11, 12 and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e. domains, which are also present in HIV-TAT because lysine is present in HIV TAT. As in the preceding rejections, the targeting ligand is considered to be an attached efficiency group.

Thus Cristiano anticipates the claims.

Claims 1, 11, 12, 19-21, 23-25, and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Puls et al (Gene Therapy 6: 1774-1778, 1999), as evidenced by http://www.genlantis.com/catalog/product_line.cfm?product_family_key=13&product_line_key=54, retrieved from the internet on 9/2/05.

Puls taught non-covalent complexes of polylysine and plasmid pGeneGrip encoding green fluorescent protein (GFP) under the control of a CMV promoter and a selectable marker (see map on second page of attached product information downloaded from the web site cited above). The polylysine comprised an attached antibody targeting ligand. See abstract. Regarding claims 11, 12 and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e. domains, which are also present in HIV-TAT because lysine is present in HIV TAT.

Thus Puls anticipates the claims.

Response to Arguments

Applicant's arguments filed 12/7/05 have been fully considered but they are not persuasive.

Applicant addresses the rejection over Illum at pages 15 and 16 of the response, and argues that Illum does not teach an "efficiency group". Applicant asserts that an efficiency group enhances the efficiency of cell membrane penetration, referring to Fig. 1 for support. This is unpersuasive, because the Examiner is unable to find in Fig. 1, or

in the specification as a whole, any limiting definition of the term "efficiency group". As a result, this term has been given its broadest reasonable interpretation, i.e. any group that is in any way related to efficiency. The PEG group of Illum is considered to be an "efficiency group" because it would reasonably be expected to increase the half life of the complex in circulation, thereby increasing the efficiency of the complex. Applicant argues that PEG cannot be an efficiency group because it does not enhance cell membrane penetration. This is unpersuasive because Applicant has not pointed to any place in the specification or the prior art that supports limiting the definition of "efficiency group" to groups that enhance cell membrane penetration.

Applicant addresses the rejection over Wu at pages 16-18 of the response. Applicant argues that Wu fails to teach a positively charged backbone and two members selected from the five groups set forth in claim 1. This is unpersuasive, because Wu teaches complex between polylysine and pSV2-CAT. This complex meets the limitations of species iii/iv because pSV2-CAT comprises the DNA required by group member 'iii', and the DNA encoding the persistence factor required by group member 'iv'. Wu can be interpreted to anticipate the claims in at least two ways. In the first, the first, group member 'iv' is considered to be the strand of DNA that encodes the selectable marker beta lactamase, and group member 'iii' is considered to be the complementary DNA strand. In the second, distinct plasmids are considered to be the two members, since each plasmid comprises both DNA, and DNA encoding a persistence factor. Because one of skill in the art appreciates that polyplexes of plasmid DNA and polylysine generally contain a plurality of plasmids, absent evidence

to the contrary the complexes of Wu contain more than one plasmid. Since each plasmid contains both DNA, and DNA encoding a persistence factor, Wu anticipates the claims. Also note that the polylysine of Wu also comprises positively charged branching groups that are fragments of HIV-TAT, i.e. the positively charged lysine side chains.

Applicant also argues that the asialoglycoprotein targeting ligand of Wu is not an "efficiency group" because it does not appear to enhance the efficiency of transport through the cell membrane. This is unpersuasive for several reasons. First, as indicated above, Applicant has failed to point to any limiting definition in the specification of the term "efficiency group", and so there is no support for arbitrarily limiting the definition of this term to groups that enhance the efficiency of transport through the cell membrane. However, even if there was support for this arbitrary definition, the argument that a targeting ligand fails to enhance the efficiency of transport is unpersuasive. Targeting ligands allow complexes to be taken up into cells by receptor mediated endocytosis. Applicant has provided no evidence or logic to demonstrate that this does not result in an increase in uptake efficiency of the complex by the targeted cells. In contrast, Fig. 3 of Wu provides objective evidence that the presence of the targeting ligand on polylysine increased uptake and expression of plasmid DNA over that seen with non-targeted polylysine. Compare lanes 2 and 4.

Applicant addresses the rejection over Cristiano at pages 18 and 19 of the response. Applicant does not see where Cristiano teaches a positively charged backbone and at least 2 members of the five members of group b wherein at least one

member is selected from groups i, iii, and v. Similarly to Wu above, Cristiano taught targeting ligand-modified polylysine, wherein the targeting ligand is reasonably interpreted as an efficiency group because it mediates uptake by the appropriate target cells. Also similarly to Wu, Cristiano taught plasmid DNAs that are members of both groups iii and iv. The plasmids contain a strand encoding a selectable marker, considered to be a persistence factor, and a complementary strand that fulfills the DNA limitation of group iii. Furthermore, the adenovirus of Cristiano also comprises a DNA that is separate and distinct from the plasmid DNA encoding the persistence factor. This DNA fulfills the limitation of group iii. Finally , absent evidence to the contrary, the adenovirus of Cristiano also encodes adenoviral preterminal protein, which is the only example of a persistence factor given in the instant specification. So Cristiano taught an embodiment in which the plasmid DNA corresponds to group member iii, and the adenoviral DNA corresponds to group member iv.

Applicant also argues that Cristiano does not "teach, disclose, or suggest "[an] efficiency group [that] is selected from the group consisting of (Gly)n1-(Arg)n2, wherein the subscript n1 is an integer from 3 to about 5, and the subscript n2 is an odd integer of from about 7 to about 17, and TAT domains" as recited in Applicant's independent claim 19 and corresponding dependent claims 20, 23-25, and 27." This is unpersuasive because any two lysine residues of the polylysine of Cristiano can be considered to be attached efficiency groups that correspond to an HIV-TAT domain. Evidence that HIV-TAT contains tandem lysines comes from instant SEQ ID NO: 20. Finally, the side

chains of the polylysine could be considered to be positively charged branching groups that are present in TAT, and therefore fulfill the limitation "TAT domains".

Applicant addresses the rejection over Puls at page19 and 20 of the response. Applicant does not see where Puls teaches a positively charged backbone and at least 2 members of the five members of group b wherein at least one member is selected from groups i, iii, and v. Similarly to Wu above, Puls taught targeting ligand-modified polylysine, wherein the targeting ligand is reasonably interpreted as an efficiency group because it mediates uptake by the appropriate target cells. The polylysine also comprises positively charged branching groups that are fragments of HIV-TAT, i.e. the positively charged lysine side chains. Also, any two lysine residues of the polylysine of Cristiano can be considered to be attached efficiency groups that correspond to an HIV-TAT domain. Evidence that HIV-TAT contains tandem lysines comes from instant SEQ ID NO: 20. Also similarly to Wu, Puls taught plasmid DNAs that are members of both groups iii and iv. The plasmids contain a strand encoding a selectable marker, considered to be a persistence factor, and a complementary strand that fulfills the DNA limitation of group iii.

Applicant argues that Puls does not teach a "non-covalent association complex" because the targeting ligand is covalently attached to the polylysine. This is unpersuasive, because the targeting ligand of Puls is considered to be an efficiency group, as in the rejections over Wu and Cristiano. The instant claims do not exclude covalent attachment of efficiency groups to the positively charged backbone, and it is unclear how such groups are intended to be attached if not covalently. The

specification does not teach attachment of efficiency groups to the positively charged backbone by charge interaction.

For these reasons the rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10-12, 19-21, 23, 24, 27 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US Patent 5,744,166) in view of the 1998 Promega Catalog.

Illum taught non-covalent complexes of polycations and nucleic acids encoding genes. One exemplary polycation is DEAE-dextran of molecular weight 5000 to 40 $X10^6$ Da, another is polylysine. See abstract; column 3, lines 16-32, and 57.

Illum did not require that the DNA must encode a persistence factor, or specify any relationship between the length of the polycation and the length of the nucleic acid.

One of ordinary skill in the art appreciates that in order to obtain expression of a gene, the gene must be operably linked to expression control sequences such as a promoter. This is conveniently achieved by inserting a gene of interest into a plasmid expression vector, such as the mammalian expression vectors disclosed at pages 262-265 of the 1998 Promega catalog. These plasmids have the added advantage of

selectable markers that allow amplification of the plasmid in bacterial cells or selection of transfectants in mammalian cells. For the purpose of this rejection, selectable markers are considered to be persistence factors, as recited in claim 1. Furthermore, the SV40 poly A sites in each of the disclosed vectors are considered to be persistence factors inasmuch as they play a role in stabilizing expressed mRNAs, and the plasmid replication origins are also considered to encode persistence factors inasmuch as they allow replication of the plasmids. Note also that three of the four vectors include CMV promoter/enhancers.

It would have been obvious to one of ordinary skill in the art at the time of the invention to insert a gene of Illum into any one of the expression vectors disclosed by Promega, prior to incorporation into the composition of Illum. One would have been motivated to do so because such plasmids facilitate handling of nucleic acids by allowing amplification in bacterial hosts prior to delivery to mammalian hosts.

Illum taught a range of DEAE-dextran of molecular weights from 5000 to 40 $X10^6$ Da. Assuming a monomer molecular weight of about 217 Da per monomer, this corresponds to DEAE-dextran lengths of about 23 to about 184000 monomers. The "preferred " molecular weight of 500,000 Da corresponds to about 2300 monomers. The monomer lengths of the Promega plasmids carrying an average gene of 2 kb would range from about 5.6 to about 7.8 kb. It would have been obvious to one of ordinary skill in the art, as a matter of routine optimization to select the length of DEAE dextran that gave the optimal transfection efficiency for a given plasmid DNA. Absent evidence of unexpected results it would have been obvious to arrive at a length of DEAE-dextran,

in monomers, in the range of about 1 to about 4 times the length the plasmid DNA in base pairs.

With regard to claim 11, note that DEAE-dextran is a polymer comprising attached positively charged branching groups.

With regard to claims 11 and 12, Note that Illum also exemplified polylysine as a polycation for use in the invention. Polylysine is a polymer comprising attached positively charged branching groups which are also present in HIV-TAT because lysine is present in HIV TAT. Use of polylysine in the formation of complexes with plasmid DNAs comprising selectable markers would render claims 1, 11 and 12 obvious.

Further, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the elements of the invention of Illum into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Thus the invention as a whole was prima facie obvious.

Claims 19, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Puls et al (Gene Therapy 6: 1774-1778, 1999) in view of Luo et al (US Patent 6,280,937) and http://www.genlantis.com/catalog/product_line.cfm?product_family_key=13&product_line_key=54, retrieved from the internet on 9/2/05.

Puls taught non-covalent complexes of polylysine and plasmid pGeneGrip encoding green fluorescent protein (GFP) under the control of a CMV promoter and a

selectable marker (see map on second page of attached product information downloaded from the web site cited above). The polylysine comprised an attached antibody targeting ligand which is considered to be an efficiency group. See abstract. Regarding claims 11, 12 and 21, polylysine is a polymer comprising attached positively charged branching groups, i.e. domains, which are also present in HIV-TAT because lysine is present in HIV TAT.

Puls did not teach a nucleic acid encoding blue fluorescent protein.

Luo taught that blue fluorescent protein and green fluorescent proteins could be used as alternative markers for detection. See column 6, lines 45-57. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

Thus the invention as a whole was prima facie obvious.

Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al (J. Biol. Chem. 262(10): 4429-4432, 1987) in view of GenBank Accession No. M77788 (2005).

Wu taught non-covalent complexes of plasmid pSV2 CAT and polylysine, wherein the polylysine comprised an attached asialoorosomucoid targeting ligand. See abstract. Plasmid pSV2 CAT comprises a selectable marker (beta lactamase, i.e. ampicillin resistance) as evidenced by GenBank Accession No. M77788. The selectable marker is considered to be a persistence factor as required by claim 39.

Wu did not teach organization of the polycation and nucleic acid into a kit.

It would have been obvious to one of ordinary skill in the art at the time of the invention to organize the elements of the invention of Wu into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 12/7/05 have been fully considered but they are not persuasive.

Applicant addresses the rejection over Illum in view of Promega at pages 20-22 of the response. Applicant argues that the combined references do not teach the claimed invention. However, as discussed above under 102 and 103 rejections, Illum teaches all of the elements of the claimed invention except that Illum did not require that the DNA must encode a persistence factor, or specify any relationship between the length of the polycation and the length of the nucleic acid. Illum also did not teach a kit. Promega taught plasmid DNAs encoding persistence factors, and it would have been

obvious to use them in the compositions of Illum because the plasmids facilitate handling of nucleic acids by allowing amplification in bacterial hosts prior to delivery to mammalian hosts. In using the plasmids, the limitations of claim 10 would be met due to the length of the polycation of Illum and the lengths of the plasmids of Promega, as discussed in detail in the rejection. Applicant has not directly addressed this portion of the rejection. It also would have been obvious to organize the elements of the invention of Illum into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors. For these reasons the rejection is maintained.

Applicant addresses the rejection over Puls in view of Luo at page 22 of the response. Applicant's arguments are based on the position that Puls does not teach the composition of claim 19, and Luo does not alleviate this deficiency. This is unpersuasive for the reasons set forth above under 102 rejections, i.e. Puls anticipates claim 19. Applicant has not argued presented any reason why the references are not combinable, so the rejection is maintained.

Conclusion

No claim is allowed. Claims 2-4 are objected to as depending from a rejected claim but would be allowable if rewritten in independent form incorporating all the limitations of claim 1.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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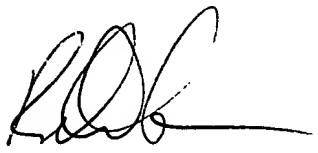

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635

S22662	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and efficiency	2006-02-27 09:10:34
S22661	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and domain	2006-02-27 08:28:34
S22660	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and efficien$	2006-02-27 07:25:10
S22659	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and biological same agent	2006-02-24 14:43:12
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S22657	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and transgen$	2006-02-24 13:58:33
S22656	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(polylysine or poly lysine or poly l lysine) same tat	2006-02-24 10:33:15
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S22654	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and vegf	2006-02-24 10:07:12
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S22652	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20030229034.pn. and arg$	2006-02-24 07:49:10
S22651	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	5945290.pn.	2006-02-23 10:45:38